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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,393	12/21/2001	Stephen Quirk	11301-1170 (44039-250928)	1033

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EXAMINER	
SWOPE, SHERIDAN	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 12/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/026,393	QUIRK ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *September 26, 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *62-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *62-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

Applicant's response, on September 26, 2005 to the RCE/First Action on the Merits of this case mailed May 25, 2005, is acknowledged. It is acknowledged that applicants have cancelled all pending claims, Claims 1-61, and added Claims 62-81. New Claims 62-81 are deemed to be encompassed by the elected invention, a method for detecting a protease. Claims 62-81 are pending and are hereby considered.

Specification

Objection to the specification for failing to define the abbreviation "SPDP" on page 15, line 3, is maintained, as no correction or arguments have been made.

The specification is objected to for failing to provide the full citation for Levy et al, Odake et al, and Su et al, which are referred to on page 2, paragraph 4.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 USC 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 63-81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons below.

For Claim 62, the phrase "tissue inhibitor" renders the claim indefinite. Said phrase is not defined by the claims or the specification and, thus, one of ordinary skill in the art would not

be reasonably appraised of the metes and bounds of the recited invention. Claims 63-81, as dependent from Claim 62, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the same reasons. For purposes of examination, it is assumed that said phrase means "Tissue Inhibitors of MetalloProteinase (TIMP)", as defined in the specification (pg 2, parg 2).

For Claim 80, the phrase "the sample reservoir" lacks antecedent basis. A person of ordinary skill in the art would not know the metes and bounds of the recited invention. Claim 81, as dependent from Claim 80, is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the same reason.

For Claim 81, the phrase "each reaction site" lacks antecedent basis. A person of ordinary skill in the art would not know the metes and bounds of the recited invention.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

In this regard, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4)

the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claims 62, 63, 65, 66, 68-81 are rejected under 35 U.S.C. 112, first paragraph, for lack of enablement. The specification is enabling for a method of detecting a metalloprotease and selecting a TIMP inhibitor of the detected metalloprotease, if the detected metalloprotease was known, at the time of filing of the instant application, to be inhibited by one or more of TIMP-1, TIMP-2, TIMP-3, and TIMP-4, the TIMPs which were known at the time of filing (Brew et al, 2000). However, the specification does not reasonably provide enablement for a method of detecting any metalloproteinase and then selecting a TIMP that inhibits said any metalloproteinase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 62, 63, 65, 66, 68-81 are so broad as to encompass a method for detecting any protein with metalloproteinase activity and then selecting an inhibitor of the detected metalloproteinase, wherein the inhibitor is a TIMP. The scope of these claims is not commensurate with the enablement provided by the disclosure with regard to detecting any one of the large number of metalloproteinases encompassed and then selecting a TIMP inhibitor for the detected metalloproteinase.

The specific reagents and steps used for immuno-detection of any metalloproteinase are well known in the art. However, not all proteins with metalloproteinase activity were known to

be inhibited by one or more of TIMP-1, TIMP-2, TIMP-3, and TIMP-4. Moreover, it is not routine in the art to screen the essentially unlimited number of encompassed metalloproteases for inhibition by any known TIMP or variant thereof. Predictability of which of TIMP-1, TIMP-2, TIMP-3, or TIMP-4, or variant thereof, can inhibit a specific metalloproteinase or how any TIMP can be modified to produce an inhibitor of a specific metalloproteinase requires a knowledge of, and guidance with regard to how the structure of any TIMP relates to its ability to function as an inhibitor of any specific metalloproteinase. However, in this case the disclosure is limited to detecting the presence of the matrix metalloproteinases (MMP) MMP-1, MMP-8, and MMP-9 (Example 1) and selecting one or more of TIMP-1, TIMP-2, TIMP-3, and TIMP-4 as an inhibitor.

The specification does not support the broad scope of Claims 62, 63, 65, 66, 68-81, which encompasses a method for detecting any protein with metalloproteinase activity and then selecting an inhibitor of the detected metalloproteinase, wherein the inhibitor is a TIMP. The specification does not support the broad scope of Claims 62, 63, 65, 66, 68-81 because the specification does not establish: (A) which metalloproteinases can be inhibited by TIMP-1, TIMP-2, TIMP-3, or TIMP-4; (B) how any said TIMP can be modified to produce an inhibitor of any specification metalloprotease; (C) a rational and predictable scheme for selecting a known TIMP, or variant thereof, as an inhibitor of any specific metalloprotease; and (D) the specification provides insufficient guidance as to how to successfully select a TIMP inhibitor of the essentially infinite possible choices of proteins having metalloprotease activity that can be immuno-detected.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a method for detecting any metalloproteinase and then selecting an inhibitor of the detected metalloproteinase, wherein the inhibitor is a TIMP. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of any protein with metalloprotease activity and selecting a TIMP-type inhibitor thereof is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claims 62, 63, 65, 66, 68-81 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of methods for detecting any protein with metalloproteinase activity and then selecting a TIMP that inhibits said any metalloproteinase. The specification teaches only three representative species of such methods, where MMP-1, MMP-8, or MMP-9 is detected and one or more of TIMP-1, TIMP-2, TIMP-3, or TIMP-4 is selected as an inhibitor. Moreover, the specification fails to describe any other representative species of methods for detecting a metalloproteases and selecting a TIMP inhibitor thereof by any additional identifying characteristics or properties. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to

sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 USC 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 62-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sorsa et al, 1998 in view of Stratmann et al, 2001 and further in view of Golub et al, 1997. As described in the prior actions, Sorsa et al teach a method for detecting, in a sample of fluid from a chronic, periodontal wound, the matrix metalloproteinase-8 (MMP-8). The method of Sorsa et al uses an immuno-chromatographic lateral flow technique. A first target antibody to MMP-8 is coated onto particles and acts a label that can be detected, for example, by its fluorescent or chemiluminescent properties. The particles can be polystyrene (col 13, parg 3). In the method of Sorsa et al, a sample of gingival crevicular fluid from a patient with periodontal disease is applied to a reservoir of a capillary support/absorbent membrane system. The label/target antibody/particles, which are applied to the membrane, migrate by diffusion coming in contact with and binding any MMP-8 in the sample. Further diffusion of the label/target antibody/particle/MMP-8 complex brings the complex into contact with a second capture antibody that has been attached in a zone-like reaction site within the membrane. When the liquid flow carrying the complex migrates through this zone, label/target antibody/particle complexes that contain MMP-8 are bound to the reaction site zone via the capture antibody.

Thus, the zone is detected if MMP-8 is present in the sample (Abstract; col 22, lines 19-45). A person of ordinary skill in the art would know that, since the process of migration occurs by diffusion, at the end of the membrane there is an area that collects buffer and reactants not bound to the reaction zone. The method of Sorsa et al uses antibodies that specifically recognize the active or proform of MMP-8 (col 10, parg 3; col 14, parg 4-5). Sorsa et al do not teach selecting a TIMP inhibitor of the detected MMP-8. However, TIMP inhibitors of MMP-8 were known in the art; for example, Stratmann et al teach that TIMP-4 inhibits MMP-8 (Table 2). It would have been obvious to a person of ordinary skill in the art to extend the method of Sorsa et al by selecting TIMP-4 as an inhibitor of MMP-8. Motivation to do so is provided by Golub et al wherein they teach that treatment of periodontal patients with a MMP-8 inhibitor (Figs 3 & Table 2) reduces degradation of periodontal collagen (Fig 1 & 2). The expectation of success is high, as immuno-diffusion methods for detecting proteins as well as selecting an inhibitor of an enzyme known to cause a disease or disorder are common in the art. Therefore, Claims 62-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sorsa et al, 1998 in view of Stratmann et al, 2001 and further in view of Golub et al, 1997.

Claims 79-81 are rejected under 35 USC 103(a) as being unpatentable over Sorsa et al, 1998 in view of Rowe et al, 1999 and further in view of Stratmann et al, 2001 or Brew et al, 2000, and Sodek et al, 1992. The teachings of Sorsa et al are described above. Sorsa et al do not teach a method for simultaneously detecting a plurality of metalloproteinases in a sample. Rowe et al teach a method for detecting a plurality of proteins in a mixed sample using an array of capture antibodies specific for three different proteins. After incubation with the mixed sample, the binding of each specific protein to its respective capture antibody is detected by a

fluorescently-labeled target antibody, which binds to the same specific protein. In this manner, the presence of each of a plurality of proteins in a mixed sample is detected (Fig 4). It would have been obvious to a person of ordinary skill in the art to incorporate the array approach of Rowe et al into the methods of Sorsa et al. In such a combined method, a sample of gingival crevicular fluid from a patient with periodontal disease comprising a plurality of metalloproteases, for example a combination of MMP-1, MMP-2, MMP-3, MMP-8, and/or MMP-9, would be reacted with particle-bound fluorescent or chemiluminescent target antibodies specific for each protease. Then diffusion of the label/target antibody/particle/metalloprotease complex would bring the complex into contact with an array of second, protease-specific capture antibodies, allowing detection of each specific metalloproteinase. After detection, one of TIMP-1, which inhibits MMP-1, MMP-2, and MM-3 (Brew et al; Table 1), or TIMP-4, which inhibits MMP-8 and MMP-9 (Stratmann et al; Table 2), would be selected as an inhibitor. Motivation to do so is derived from the fact that metalloproteases are involved in periodontal disease (Sodek et al, 1992; Abstract, Figs 2 & 3) and the array would allow efficient determination of which proteases are present in patient samples. It is noted that the expectation of success for this method depends on knowing which, if any, TIMP inhibits a specific metalloprotease (see rejection of Claims 62, 63, 65, 66, 68-81 under 35 U.S.C. 112, first paragraph, for lack of enablement, above). However, if a specific metalloprotease was known to be inhibited by one or more specific TIMPs, or a specific variant thereof, the expectation of success is high, as (i) the use of capture-antibody arrays to detect a plurality of proteins, (ii) the combined use of first, target antibodies and second, capture antibodies to detect metalloproteases, and (iii) selecting a TIMP inhibitor of a MMP are all known in the art. Therefore, Claims 79-81 are rejected under

35 USC 103(a) as being unpatentable over the combination of Sorsa et al, 1998 in view of Rowe et al, 1999 and further in view of Stratmann et al, 2001 or Brew et al, 2000, and Sodek et al, 1992.

In support of their request that the prior rejection of Claims 46-52 and 54-59 under 35 USC 102(b), as being anticipated by Sorsa et al, 1998 be withdrawn, Applicants provide the arguments below. Said arguments are moot in terms of the prior rejection of Claims 46-52 and 54-59, because said claims have been cancelled. Nonetheless, their relevance to the rejection of Claims 62-81 35 USC 103(a) herein is addressed.

(A) The Office cites Sorsa et al, US patent 5,736,341, as anticipating original independent claim 46. As noted in Applicants' previous response, Sorsa et al is specific to the use of a saliva sample, a mouthrinse sample, or a sample of gingival crevicular fluid to diagnose whether or not a patient has periodontal disease. However, this is not a "chronic wound" as would be understood to one of ordinary skill in the art, e.g., an open cutaneous wound, burn wound, neuropathic ulcer, pressure sore, venous stasis ulcer, or diabetic ulcer.

(B) Sorsa et al also fails to disclose other limitations of independent claim 62. For example, the selection of a tissue inhibitor that inhibits the activation or activity of the identified metalloproteinase.

(C) The recited method is a rapid and accurate detection method, which allows for the immediate selection of a tissue inhibitor that is specific for the identified metalloproteinase. The method allows for treatment of *current* condition, without waiting several days for a result (Applicants' emphasis).

These arguments are not found to be persuasive for the following reasons.

(A) Reply: As acknowledged by Applicants' this is the same argument set forth in their prior responses. Applicants are directed to the Examiner's reply regarding the definition of "chronic wound" and its relevance to periodontal disease (Final Rejection of January 1, 2005 and the RCE/First Action on the Merits of May 25, 2005). Applicants are particularly referred to Wikesjo et al, 2000 (Periodontal wound healing and regeneration. *Periodontology* Vol 19: pg 21-39; esp pg 22, parg 1-2 – provided with the Final Rejection), and Bergstrom et al, 2004 (Tobacco smoking and chronic destructive periodontal disease. *Odontology* Vol 92(1): pg 1-8, esp Abstract – cited within the RCE/First Action, pg 5 therein).

It is acknowledged that Sorsa et al, teach using a general saliva sample or a mouthrinse sample. However, they also teach using a sample collected from gingival crevicular fluid associated with a specific lesion (col 11, parg 7).

(B) Reply: It is acknowledged that Sorsa et al fails to disclose the selection of a TIMP that inhibits the activation or activity of their identified metalloproteinase. Therefore, Claims 62-81, comprising said limitation, are rejected herein under 35 U.S.C. 103(a), using Sorsa et al, 1998 as the primary reference.

(C) Reply: It is acknowledged that the recited method is a rapid and accurate means to detect a metalloprotease and select an inhibitor. The method of Sorsa et al, is also rapid and accurate (col 10, parg 5) and, if a TIMP inhibitor for the specific metalloprotease where known in the art, a skilled artisan would have been able to rapidly and accurately select a TIMP inhibitor for the specific metalloprotease detected.

For these reasons and those discussed in the prior actions, Claims 62-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sorsa et al, 1998 in view of Stratmann et al,

2001 and further in view of Golub et al, 1997, while Claims 79-81 are rejected under 35 USC 103(a) as being unpatentable over Sorsa et al, 1998 in view of Rowe et al, 1999, and further in view of Stratmann et al, 2001 or Brew et al, 2000, and Sodex et al, 1992.

Claims 62-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trengove et al, 1999 in view of Sorsa et al, 1998 and further in view Stratmann et al, 2001 and Brew et al, 2000. Trengove et al teach using an enzymatic assay for detecting metalloproteases in the fluid of chronic wounds including diabetic foot ulcers, mixed vessel disease ulcers, and decubitus ulcers (pg 444, parg 2; Figs 1-3). Trengove et al do not teach an immuno-diffusion method for detecting any specific metalloprotease in the fluid of chronic wounds using a target antibody, a signal element, and a capture antibody. As described above, Sorsa et al teach an immuno-chromatographic lateral flow method for detecting a specific metalloproteinase. It would have been obvious to a person of ordinary skill in the art to use the immuno-chromatographic lateral flow method of Sorsa et al to identify metalloproteases in the chronic wounds studied by Trengove et al. Motivation to do so is provided by Trengove et al, wherein they state that specific metalloproteases, including MMP-9, MMP-2, and neutrophil elastase, contribute to the pathophysiology of chronic wounds (pg 443, parg 5-6). Neither Trengove et al nor Sorsa et al, or a combination thereof, teach, after detection of a metalloprotease, selecting a TIMP inhibitor thereof. However, TIMP inhibitors of metalloproteases were known in the art. For example Brew et al teach that TIMP-1 inhibits MMP-1, MMP-2, and MMP-3 (Table 1), while Stratmann et al teach that TIMP-4 inhibits MMP-8 and MMP-9 (Table 2). Thus, it would be obvious to a person of ordinary skill in the art to select a TIMP inhibitor of an identified metalloprotease. Motivation to do so is derived from the desire to treat chronic wounds with inhibitors of the

metalloproteases found therein, including TIMPs (Trengove et al, pg 450, parg 9 – pg 451, parg 1; pg 443, parg 2-4). Again, the expectation of success for this method depends on knowing which, if any, TIMP inhibits a specific metalloprotease. However, if a specific metalloprotease was known to be inhibited by one or more specific TIMPs, or a specific variant thereof, the expectation of success is high, as immuno-chromatographic lateral flow techniques, using a target antibody, a signal element, and a capture antibody, for analyzing metalloprotease in bodily fluids as well as selecting a TIMP known to inhibit a specific MMP are known in the art. Therefore, Claims 62-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trengove et al, 1999 in view of Sorsa et al, 1998 and further in view Stratmann et al, 2001 and Brew et al, 2000.

Claims 79-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trengove et al, 1999 in view of Sorsa et al, 1998 and Rowe et al, 1999 and further in view of Stratmann et al, 2001 and Brew et al, 2000. The teachings of Trengove et al, Sorsa et al, Stratmann et al, and Brew et al are described above. Neither Trengove et al, Sorsa et al, Stratmann et al, and Brew et al, or a combination there of, teach a method for detecting a plurality of metalloproteases. As described above, Rowe et al teach an immuno-array method for detecting a plurality of proteins. It would have been obvious to a person of ordinary skill in the art to use the array approach of Rowe et al to expand on the method of Sorsa et al in order to identify a plurality of metalloproteases, for example MMP-1, MMP-2, MMP-3, MMP-8, and MMP-9, in the fluid from chronic wounds studied by Trengove et al. Then, one of TIMP-1, which inhibits MMP-1, MMP-2, and MM-3 (Brew et al; Table 1), or TIMP-4, which inhibits MMP-8 and MMP-9 (Stratmann et al; Table 2), would be selected as an inhibitor. Motivation to do so is derived from the desire

to determine which metalloproteases are found in the wound in order to select an inhibitor of the metalloprotease, such as a TIMP (Trengove et al, pg 450, parg 9 – pg 451, parg 1; pg 443, parg 2-4). Again, the expectation of success for this method depends on knowing which, if any, TIMP inhibits a specific metalloprotease. However, if a specific metalloprotease was known to be inhibited by one or more specific TIMPs, or a specific variant thereof, the expectation of success is high, as (i) immuno-chromatographic lateral flow techniques, using a target antibody, a signal element, and a capture antibody, for analyzing metalloprotease in bodily fluids, (ii) immuno-array methods for detecting proteins, and (iii) selecting a TIMP known to inhibit a specific MMP are known in the art. Therefore, Claims 79-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Trengove et al, 1999, Sorsa et al, 1998, and Rowe et al, 1999 and further in view of Stratmann et al, 2001 and Brew et al, 2000.

It is noted that Claims 46-52 and 54-59 were rejected in the RCE/First Action of May 25, 2005 under 35 U.S.C. 103(a) as being unpatentable over Trengove et al, 1999 in view of Sorsa et al, 1998, while Claims 53, 60, and 61 were rejected in said action under 35 U.S.C. 103(a) as being unpatentable over Trengove et al, 1999 in view of Sorsa et al, 1998 and further in view of Rowe et al, 1999. Applicants did not comment on said rejections, which are relevant to the rejection herein of Claims 62-78 under 35 U.S.C. 103(a) as being unpatentable over Trengove et al, 1999 in view of Sorsa et al, 1998 and further in view of Stratmann et al, 2001 and Brew et al, 2000 as well as the rejection herein of Claims 79-81 under 35 U.S.C. 103(a) as being unpatentable over Trengove et al, 1999 in view of Sorsa et al, 1998 and Rowe et al, 1999 and further in view of Stratmann et al, 2001 and Brew et al, 2000.

Applicant's amendment necessitated any new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Regarding filing an Appeal, Applicants are referred to the Official Gazette Notice published July 12, 2005 describing the Pre-Appeal Brief Review Program.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheridan Lee Swope, Ph.D.

Art Unit 1656

SHERIDAN SWOPE, Ph.D.
PATENT EXAMINER